

IFWP

RAW SEQUENCE LISTING DATE: 07/10/2006
PATENT APPLICATION: US/10/584,810 TIME: 10:24:35

Input Set : A:\21471 SEQ LSTG 6 16 06.TXT
Output Set: N:\CRF4\07102006\J584810.raw

```
4 <110> APPLICANT: Merck & Co., Inc.
      6 <120> TITLE OF INVENTION: HCV RNA-DEPENDENT RNA POLYMERASE
     9 <130> FILE REFERENCE: 21471 PCT
C--> 11 <140> CURRENT APPLICATION NUMBER: US/10/584,810
C--> 11 <141> CURRENT FILING DATE: 2006-06-28
    11 <150> PRIOR APPLICATION NUMBER: 60/535,708
     12 <151> PRIOR FILING DATE: 2004-01-09
     14 <160> NUMBER OF SEQ ID NOS: 28
    16 <170> SOFTWARE: FastSEQ for Windows Version 4.0
    18 <210> SEQ ID NO: 1
    19 <211> LENGTH: 571
    20 <212> TYPE: PRT
    21 <213> ORGANISM: Artificial Sequence
    23 <220> FEATURE:
     24 <223> OTHER INFORMATION: modified HCV NS5B
    26 <400> SEQUENCE: 1
    27 Met Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ser
                                           10
     29 Pro Glu Glu Lys Leu Pro Ile Asn Pro Leu Ser Asn Ser Leu Leu
                   20
                                       25
    31 Arg Tyr His Asn Lys Val Tyr Cys Thr Thr Lys Ser Ala Ser Leu
                                   40
     33 Arg Ala Lys Lys Val Thr Phe Asp Arg Met Gln Val Leu Asp Ser Tyr
     35 Tyr Asp Ser Val Leu Lys Asp Ile Lys Leu Ala Ala Ser Lys Val Thr
                           70
     37 Ala Arg Leu Leu Thr Met Glu Glu Ala Cys Gln Leu Thr Pro Pro His
     39 Ser Ala Arg Ser Lys Tyr Gly Phe Gly Ala Lys Glu Val Arg Ser Leu
                                       105
     41 Ser Gly Arg Ala Val Asn His Ile Lys Ser Val Trp Lys Asp Leu Leu
                                   120
            115
    43 Glu Asp Ser Glu Thr Pro Ile Pro Thr Thr Ile Met Ala Lys Asn Glu
    44 130
                               135
     45 Val Phe Cys Val Asp Pro Thr Lys Gly Gly Lys Lys Ala Ala Arg Leu
                           150
                                                155
     47 Ile Val Tyr Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu
                                           170
                       165
    49 Tyr Asp Ile Thr Gln Lys Leu Pro Gln Ala Val Met Gly Ala Ser Tyr
                                       185
    51 Gly Phe Gln Tyr Ser Pro Ala Gln Arg Val Glu Phe Leu Leu Lys Ala
                                   200
    53 Trp Ala Glu Lys Lys Asp Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys
```

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```
54
      210
                          215
55 Phe Asp Ser Thr Val Thr Glu Arg Asp Ile Arg Thr Glu Glu Ser Ile
                      230
                                          235
57 Tyr Arg Ala Cys Ser Leu Pro Glu Glu Ala His Thr Ala Ile His Ser
                                      250
                  245
59 Leu Thr Glu Arg Leu Tyr Val Gly Pro Met Phe Asn Ser Lys Gly
                                  265
              260
61 Gln Thr Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr
                              280
63 Ser Met Gly Asn Thr Ile Thr Cys Tyr Val Lys Ala Leu Ala Ala Cys
                          295
65 Lys Ala Ala Gly Ile Ile Ala Pro Thr Met Leu Val Cys Gly Asp Asp
                      310
                                          315
67 Leu Val Val Ile Ser Glu Ser Gln Gly Thr Glu Glu Asp Glu Arg Asn
                                      330
                  325
69 Leu Arg Ala Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly
              340
                                  345
71 Asp Pro Pro Arg Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser
                              360
73 Ser Asn Val Ser Val Ala Leu Gly Pro Gln Gly Arg Arg Tyr Tyr
                          375
75 Leu Thr Arg Asp Pro Thr Thr Pro Ile Ala Arg Ala Ala Trp Glu Thr
                      390
77 Val Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr
                                      410
                  405
79 Ala Pro Thr Ile Trp Ala Arg Met Val Leu Met Thr His Phe Phe Ser
                                  425
81 Ile Leu Met Ala Gln Asp Thr Leu Asp Gln Asn Leu Asn Phe Glu Met
                              440
         435
83 Tyr Gly Ala Val Tyr Ser Val Ser Pro Leu Asp Leu Pro Ala Ile Ile
84 450
                          455
85 Glu Arg Leu His Gly Leu Asp Ala Phe Ser Leu His Thr Tyr Thr Pro
                      470
                                          475
87 His Glu Leu Thr Arq Val Ala Ser Ala Leu Arg Lys Leu Gly Ala Pro
                  485
                                      490
89 Pro Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu
              500
                                  505
91 Ile Ser Arg Gly Gly Arg Ala Ala Val Cys Gly Arg Tyr Leu Phe Asn
          515
                              520
                                                   525
93 Trp Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Arg
                          535
95 Leu Leu Asp Leu Ser Ser Trp Phe Thr Val Gly Ala Gly Gly Asp
                     550
97 Ile Tyr His Ser Val Ser Arg Ala Arg Pro Arg
                                      570
101 <210> SEQ ID NO: 2
102 <211> LENGTH: 571
103 <212> TYPE: PRT
104 <213> ORGANISM: Artificial Sequence
```

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			PAIOI													
107	7 <223> OTHER INFORMATION: modified HCV NS5B															
109	<400> SEQUENCE: 2															
110	Met	Ser	Met	Ser	Tyr	Thr	Trp	Thr	Gly	Ala	Leu	Ile	Thr	Pro	Cys	Gly
111	1				5					10					15	
112	Pro	Glu	Glu	Glu	Lys	Leu	Pro	Ile	Asn	Pro	Leu	Ser	Asn	Ser	Leu	Met
113				20	-				25					30		
	Ara	Phe	His		Lvs	۷al	Tvr	Ser		Thr	Ser	Ara	Ser	Ala	Ser	Leu
115			35		-1-		-1-	40				5	45			
	Δrα	Δla		Lve	Val	Thr	Phe		Ara	Val	Gln	Val	Leu	Asp	Δla	His
117	Arg	50	Ly S	шу 3	Vai		55	пор	*** 9	v a_	0111	60	100	1101		
	Tr.~		Sar	77-7	T.OU	Gln		V≈1	Tare	Ara	λla		Ser	Tare	Val	Ser
119	_	Asp	Ser	Val	пец	70	nsp	vai	цуз	n. 9	75	niu	DCI	Lys	•	80
		7. ~~	T 011	T 011	mh~		C1.,	C1	אן ה	Crra		T 011	Thr	Dro	Dro	
	Ala	Arg	Leu	ьeu		vai	GIU	GIU	мта	90	AIa	пец	1111	FIO	95	1113
121	0	77-	T	0	85	M	G1	Dho	~1		T	C1	1707	7.~~		T 011
	ser	Ата	ьys		Arg	TYL	GIA	Pne		АІа	цуѕ	GIU	Val		ser	цец
123	_		_	100	1				105	0	**- 7		a 1	110	T	T
	Ser	Arg		Ala	vaı	Asn	HIS		Arg	Ser	vai	Trp		Asp	Leu	Leu
125			115	•				120		1			125	_	_	~3
	Glu		Gln	His	Thr	Pro		Asp	Thr	Thr	He		Ala	Lys	Asn	Glu
127		130					135		_	_		140				_
128	Val	Phe	Cys	Ile	Asp		Thr	Lys	Gly	Gly	_	Lys	Pro	Ala	Arg	
	145					150					155					160
130	Ile	Val	Tyr	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu
131					165					170					175	
132	Tyr	Asp	Ile	Ala	Gln	Lys	Leu	Pro	Lys	Ala	Ile	Met	Gly	Pro	Ser	Tyr
133				180					185					190		
134	Gly	Phe	Gln	Tyr	Ser	Pro	Ala	Glu	Arg	Val	Asp	Phe	Leu	Leu	Lys	Ala
135			195					200					205			
136	Trp	Gly	Ser	Lys	Lys	Asp	Pro	Met	Gly	Phe	Ser	Tyr	Asp	Thr	Arg	Cys
137		210					215					220				
138	Phe	Asp	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Ser	Ile
139	225	-				230					235					240
140	Tyr	Gln	Ala	Cys	Ser	Leu	Pro	Gln	Glu	Ala	Arg	Thr	Val	Ile	His	Ser
141	•			-	245					250					255	
142	Leu	Thr	Glu	Arq	Leu	Tyr	Val	Gly	Gly	Pro	Met	Thr	Asn	Ser	Lys	Gly
143				260		•		•	265					270	_	_
	Gln	Ser	Cvs	Glv	Tvr	Ara	Arg	Cvs	Arq	Ala	Ser	Glv	Val	Phe	Thr	Thr
145	-		275	4	4	_		280	_			-	285			
	Ser	Met.		Asn	Thr	Met.	Thr	Cvs	Tvr	Ile	Lvs	Ala	Leu	Ala	Ala	Cvs
147		290	1				295	-1-	-1-		_1	300				4
	Lare		Δla	G137	T۱۵	Val		Pro	₩a1	Met	Leu		Cvs	Glv	Asp	Asp
149		niu	mru	CLY	110	310	тор	110	• • • •	1100	315	val	C _I D	0-1	1101	320
		17 a T	17-1	т10	cor		cor	Cln	C117	Λcn		Glu	Λen	Glu	Ara	Asn
	neu	vai	vai	116		GIU	SCI	GIII	GIY		GIU	GIU	ASP	O.Lu		Hom
151	T 0	7. ***	- ד ת	Dh.a	325	C1	717~	Mot	ሞኮ~	330	Ф	C0~	λ Ι ~	Dro	335 Pro	C 117
	ьeu	Arg	AIA		TIII.	GIU	ATG	MEC		Arg	TAT	Set	AId		FIO	Gly
153	70	T ~··	D	340	D	~1	Ш	n	345	a1	T	T7 -	mb	350	C*-~	Co~
	Asp	ьeu		arg	PLO	GIU	ıyr		neu	GIU	ьeu	тте	Thr	ser	Cys	261
155			355					360					365			

106 <220> FEATURE:

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156 Ser Asn Val Ser Val Ala Leu Asp Ser Arg Gly Arg Arg Tyr Phe 375 158 Leu Thr Arg Asp Pro Thr Thr Pro Ile Thr Arg Ala Ala Trp Glu Thr 159 385 390 395 160 Val Arg His Ser Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Gln Tyr 405 162 Ala Pro Thr Ile Trp Val Arg Met Val Ile Met Thr His Phe Phe Ser 420 425 164 Ile Leu Leu Ala Gln Asp Thr Leu Asn Gln Asn Leu Asn Phe Glu Met 165 435 440 166 Tyr Gly Ala Val Tyr Ser Val Asn Pro Leu Asp Leu Pro Ala Ile Ile 455 168 Glu Arg Leu His Gly Leu Glu Ala Phe Ser Leu His Thr Tyr Ser Pro 475 470 170 His Glu Leu Ser Arg Val Ala Ala Thr Leu Arg Lys Leu Gly Ala Pro 485 490 172 Pro Leu Arg Ala Trp Lys Ser Arg Ala Arg Ala Val Arg Ala Ser Leu 500 505 174 Ile Ala Gln Gly Ala Arg Ala Ile Cys Gly Arg Tyr Leu Phe Asn 520 176 Trp Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Leu Pro Glu Ala Ser 535 540 530 178 Arg Leu Asp Leu Ser Gly Trp Phe Thr Val Gly Ala Gly Gly Asp 550 179 545 180 Ile Tyr His Ser Val Ser His Ala Arg Pro Arg 565 184 <210> SEQ ID NO: 3 185 <211> LENGTH: 571 186 <212> TYPE: PRT 187 <213> ORGANISM: Artificial Sequence 189 <220> FEATURE: 190 <223> OTHER INFORMATION: modified HCV NS5B 192 <400> SEQUENCE: 3 193 Met Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr Pro Cys Ser 195 Ala Glu Glu Lys Leu Pro Ile Ser Pro Leu Ser Asn Ser Leu Leu 20 25 197 Arq His His Asn Leu Val Tyr Ser Thr Ser Ser Arg Ser Ala Ser Gln 40 199 Arg Gln Arg Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His 55 201 Tyr Lys Thr Ala Leu Lys Glu Val Lys Glu Arg Ala Ser Arg Val Lys 70 203 Ala Arg Met Leu Thr Ile Glu Glu Ala Cys Ala Leu Val Pro Pro His 85 205 Ser Ala Arg Ser Lys Phe Gly Tyr Ser Ala Lys Asp Val Arg Ser Leu 100 105 207 Ser Ser Arg Ala Ile Asp Gln Ile Arg Ser Val Trp Glu Asp Leu Leu

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: . :

209	Glu	Asp	Thr	Thr	Thr	Pro	Ile	Pro	Thr	Thr	Ile	Met	Ala	Lys	Asn	Glu
210		130	Q	** - 3		D	135	T	a 1	0 1		140	D	77-	7	T
	145	Pne	Cys	vai	Asp	150	Ala	гуѕ	GIA	GTÀ	155	ьys	PIO	Ala	Arg	160
213 214	Ile	Val	Tyr	Pro	Asp 165	Leu	Gly	Val	Arg	Val 170	Cys	Glu	Lys	Arg	Ala 175	Leu
215	Tyr	Asp	Val			Lys	Leu	Ser		-	Thr	Met	Gly		Ala	Tyr
216	~ 1	51. .	01	180	0	D	~1	~1	185	177	~ 1	7	T	190	T	Mah
217	GIY	Pne	195	Tyr	ser	Pro	Gln	200	Arg	vai	GIU	Arg	205	Leu	ьys	мес
219 220	Trp	Thr 210	Ser	Lys	Lys	Thr	Pro 215	Leu	Gly	Phe	Ser	Tyr 220	Asp	Thr	Arg	Cys
	Phe		Ser	Thr	Val	Thr	Glu	Gln	Asp	Ile	Arq		Glu	Glu	Glu	Ile
	225	-				230			-		235					240
223	Tyr	Gln	Cys	Cys	Asn	Leu	Glu	Pro	Glu	Ala	Arg	Lys	Val	Ile	Ser	Ser
224					245					250					255	
225	Leu	Thr	Glu	Arg	Leu	Tyr	Cys	Gly	Gly	Pro	Met	Phe	Asn	Ser	Lys	Gly
226				260					265					270		
227	Ala	Gln	Cys	Gly	Tyr	Arg	Arg	Cys	Arg	Ala	Ser	Gly	Val	Leu	Pro	Thr
228			275					280					285			
229	Ser		Gly	Asn	Thr	Ile	Thr	Cys	Tyr	Ile	Lys		Thr	Ala	Ala	Ala
230		290					295					300			_	_
		Ala	Ala	Gly	Leu		Asn	Pro	Asp	Phe		Val	Cys	Gly	Asp	
	305					310	_	_	~2		315	~1.	_	.		320
	Leu	vaı	vaı	vaı		GIu	Ser	Asp	GIY		Asp	GIU	Asp	Arg		Ala
234	T 011	7	. ד ג	Dho	325	C1	71-	Mot	mb~	330	Ф	Cor	ח ד ת	Dro	335	Clv
236	ьeu	Arg	Ala	340	1111	GIU	Ala	Met	345	Arg	ıyı	Ser	Ala	350	PIO	GIY
	Acn	Δ] =	Pro		Dro	Thr	Tyr	Agn		Glu	T.e.11	Tle	Thr		Cvs	Ser
238	пор	miu	355	0111	110	1111	- 7 -	360	пси	Olu	LCu		365	001	Cyb	001
	Ser	Asn		Ser	Val	Ala	Arg		Asp	Lvs	Glv	Ara		Tvr	Tvr	Tvr
240		370					375	F		-1-	1	380	5	-1-	- 1	7
241	Leu	Thr	Arg	Asp	Ala	Thr	Thr	Pro	Leu	Ala	Arg	Ala	Ala	Trp	Glu	Thr
	385		_	_		390					395			_		400
243	Ala	Arg	His	Thr	Pro	Val	Asn	Ser	Trp	Leu	Gly	Asn	Ile	Ile	Met	Tyr
244					405					410					415	
245	Ala	Pro	Thr	Ile	${\tt Trp}$	Val	Arg	Met	Val	Met	Met	Thr	His	Phe	Phe	Ser
246				420					425					430		
247	Ile	Leu	Gln	Ser	Gln	Glu	Ile	Leu	Asp	Arg	Pro	Leu	Asp	Phe	Glu	Met
248			435					440					445			
	Tyr	Gly	Ala	Thr	Tyr	Ser	Val	Thr	Pro	Leu	Asp	Leu	Pro	Ala	Ile	Ile
250		450					455					460				
		Arg	Leu	His	Gly		Ser	Ala	Phe	Thr		His	Ser	Tyr	Ser	
	465	~-7	_	_	_	470		~ 7		_	475		_	~ 3	-	480
	Val	Glu	Leu	Asn	_	Val	Ala	Gly	Thr		Arg	Lys	Leu	GLY		Pro
254	_	.			485		***		. 1 .	490	77 -	77- 7	7	n7 -	495	T
	Pro	ьeu	arg		Trp	arg	His	Arg		arg	нта	vaı	arg		гла	ьeu
256	т1.	π7 ~	~1	500	C1	T **~	~ דת	T	505	C	C1	T ~··	TT1	510	Dha	7 ~~
257	тте	Alg	GIN	стХ	стХ	гаг	Ala	ьys	тте	cys	GTÅ	neu	ı Aı.	ьеи	rile	ASII

VERIFICATION SUMMARY

DATE: 07/10/2006

PATENT APPLICATION: US/10/584,810

TIME: 10:24:36

Input Set: A:\21471 SEQ LSTG 6 16 06.TXT Output Set: N:\CRF4\07102006\J584810.raw

L:11 M:270 C: Current Application Number differs, Replaced Current Application No

L:11 M:271 C: Current Filing Date differs, Replaced Current Filing Date